

Data Evaluation Record on the Reproductive Effects of Ethylenethiourea (ETU) on Mallard Ducks (*Anas platyrhynchos*)

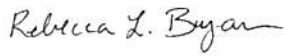
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EPA MRID Number 48819702


Data Requirement:	PMRA Data Code	{.....}
	EPA DP Barcode	402789
	OECD Data Point	{.....}
	EPA MRID	48819702
	EPA Guideline	OPPTS 850.2300

Test material: Ethylenethiourea **Purity:** 100%
Common name: Ethylenethiourea (ETU)
Chemical name: IUPAC: Not reported
CAS name: Not reported
CAS No.: Not reported
Synonyms: 2-imidazolidinethione; ETU

Primary Reviewer: Rebecca L. Bryan
Staff Scientist, CSS-Dynamac Corporation

Signature: 
Date: 5/31/13

Secondary Reviewer: John Marton, Ph.D.
Environmental Scientist, CDM Smith

Signature: 
Date: 03/13/14

Primary Reviewer: Brian Montague, Fishery Biologist
ERB 5/EFED/OPP/OSCPP/EPA

Date: March 7, 2015

Secondary Reviewer: 
ERB 5/EFED/OPP/OSCPP/EPA

Date: March 10, 2015 04/16/15

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Company Code	{.....}	[For PMRA]
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EPA PC Code	600016	

Date Evaluation Completed: {dd-mm-yyyy}

CITATION: Temple, D.L., *et al.* 2012. Ethylenethiourea: A Reproduction Study with the Mallard. Unpublished study performed by Wildlife International Ltd., Easton, MD. Laboratory Study No. 697-108. Study sponsored by EBDC/ETU Task Force, c/o McDermott, Will and Emery, Washington, D.C. Study initiated August 1, 2011 and completed April 30, 2012.

DISCLAIMER: This document provides guidance for EPA and PMRA reviewers on how to complete a data evaluation record after reviewing a scientific study concerning the reproductive effects of a pesticide on avian species. It is not intended to prescribe conditions to any external party for conducting this study nor to establish absolute criteria regarding the assessment of whether the study is scientifically sound and whether the study satisfies any applicable data requirements. Reviewers are expected to review and to determine for each study, on a case-by-case basis, whether it is scientifically sound and provides sufficient information to satisfy applicable data requirements. Studies that fail to meet any of the conditions may be accepted, if appropriate; similarly, studies that meet all of the conditions may be rejected, if appropriate. In sum, the reviewer is to take into account the totality of factors related to the test methodology and results in determining the acceptability of the study.

EXECUTIVE SUMMARY

The one-generation reproductive toxicity of Ethylenethiourea (ETU) to 16 pairs per level of 23-week old Mallard ducks (*Anas platyrhynchos*) was assessed over 20 weeks. Ethylenethiourea was administered to the birds in the diet at nominal concentrations of 0 (negative control), 4, 20, and 100 mg ai/kg diet. Mean-measured concentrations were <1.0 (<LOQ, control), 3.50, 18.2, and 100 mg ai/kg diet.

There were no treatment-related mortalities or signs of toxicity observed during the study at any dietary level. The treatment-related gross necropsy finding of enlarged thyroids was observed at 100 mg ai/kg. No effects were observed for food consumption, adult body weight, offspring body weight, or reproduction parameters at any dietary level. No significant treatment-related differences in egg shell thickness were observed between the control group and any of the treatment groups. The NOAEC was 18.2 mg ai/kg diet (mean-measured concentration) based on the necropsy finding of enlarged thyroids.

This study is scientifically sound and satisfies the guideline requirement for a Mallard (*Anas platyrhynchos*) reproductive toxicity study with the Ethylenethiourea degradate.

Results Synopsis

Test Organism Size/Age (mean Weight): 23 weeks old; 823 to 1414 g (combined sexes)

Reproductive and Growth Endpoints

LOAEL: > 100 mg ai/Kg bodyweight

NOAEL: 100 ppm

Non Reproductive Effects Noted: Enlarged Thyroid Glands

NOAEL: 18.2 mg ai/kg (mean-measured)

LOAEL: 100 mg ai/kg (mean-measured)

I. MATERIALS AND METHODS

GUIDELINE(S) FOLLOWED: U.S. EPA Pesticide Assessment Guidelines, §71-4, U.S. EPA Ecological Effects Test Guidelines OPPTS 850.2300, and OECD Test Guideline 206.

No deviations from U.S. EPA OPPTS Guideline No. 850.2300 were observed.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and No Data Confidentiality statements were provided. The study was conducted in compliance with the U.S. EPA GLP Standards (40 CFR part 160) with the exception of routine water and food contaminant screening analyses. However, the analyses were performed using laboratory standard operating procedures and standard U.S. EPA procedures.

A. MATERIALS:

1. Test Material: Ethylenethiourea (ETU)

Description: Solid

Lot No./Batch No. : XW7-102353-014

Purity: 100%

Stability of compound under test conditions: The Day 7 diet sample recoveries were 96-99% of Day 0 values.

Storage conditions of test chemicals: Ambient conditions.

Physicochemical properties of Ethylenethiourea.

Parameter	Values	Comments
Water solubility at 20°C	Not reported	
Vapor pressure	Not reported	
UV absorption	Not reported	
pKa	Not reported	
Kow	Not reported	

(OECD recommends water solubility, stability in water and light, pKa, Pow, and vapor pressure of test compound)

2. Test organism:

Table 1: Test organism

Parameter	Details	Remarks
		Criteria
Species (common and scientific names):	Mallard ducks (<i>Anas platyrhynchos</i>)	<i>Recommended species include a wild waterfowl species, preferably the Mallard (Anas platyrhynchos) or an upland game species, preferably the northern bobwhite (Colinus virginianus)</i>
Age at Study Initiation:	23 weeks old	<i>Birds approaching their first breeding season should be used.</i>
Body Weight: (mean and range)	Overall (combined sexes, combined treatments) range of 823 to 1414 g at study initiation. Adults measured at end of weeks 0,2,4,6,8 and at termination.	<i>Body weights should be recorded at test initiation and at biweekly intervals up to week eight or up to the onset of egg laying and at termination.</i>
Source:	Whistling Wings, Inc. (Hanover, IL)	Birds were phenotypically indistinguishable from wild stock. <i>All birds should be from the same source.</i>

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding study: The definitive test concentrations selected were based on a pilot reproduction study (Wildlife International Ltd., Project Number 697-106). The results of this study were not provided.

b. Definitive Study:

Table 2: Experimental Parameters

Parameter	Details	Remarks
		Criteria
Acclimation period:	5 weeks	
Conditions (same as test or not):	Not reported.	<i>Recommended observation period includes a 2-3 week health observation period prior to selection of birds for treatment. Generally, birds should be healthy without excess mortality. Feeding should be <u>ad libitum</u>, and sickness, injuries or mortality should be noted.</i>
Feeding:	Basal diet was provided daily, <i>ad libitum</i> .	
Health (any mortality observed):	Healthy birds were used in test.	
<u>Test duration</u>		
Pre-laying exposure:	10 weeks (including photo-stimulation period)	<u>Recommended pre-laying exposure duration:</u> <i>At least 10 weeks prior to the onset of egg-laying.</i> <u>Recommended exposure duration with egg-laying:</u> <i>At least 10 weeks.</i> <u>Recommended withdrawal period:</u> <i>If reduced reproduction is evident, a withdrawal period of up to 3 weeks should be added to the test phase.</i>
Egg-laying exposure:	10 weeks	
Withdrawal period, if used:	6 weeks	

Parameter	Details	Remarks
		Criteria
<u>Pen (for parental and offspring)</u> Size: Construction materials: Number:	Parental: 75 x 90 x 45 cm Offspring: 62 x 92 x 25.5 cm Vinyl-coated wire mesh. 16 parental pens/treatment level	Sisal ropes were added to each pen for animal enrichment. <u>Pens</u> <i>Pens should have adequate room and be arranged to prevent cross-contamination.</i> <u>Materials</u> <i>Recommended materials include nontoxic material and nonbinding material, such as galvanized steel.</i> <u>Number</u> <i>At least 5 replicate pens should be used for Mallards housed in groups of 7. For other arrangements, at least 12 pens should be used, but considerably more may be used if birds are kept in pairs. Chicks should be housed according to parental grouping.</i>
Number of birds per pen (male:female)	2 birds/pen (1 male:1 female)	<i>One male and one female per pen should be used. For quail, one male and two females should be used. For ducks, two males and five females should be used.</i>
<u>Number of pens per group/treatment</u> Negative control: Solvent control: Treated:	16 pens N/A 16 pens/treatment	<i>At least 12-16 pens should be used, but considerably more if birds are kept in pairs.</i>

Parameter	Details	Remarks
		Criteria
<u>Test concentrations (mg ai/kg diet)</u> Nominal: Measured:	0 (control), 4, 20, and 100 mg ai/kg diet <1.0 (<LOQ, control), 3.50, 18.2, and 100 mg ai/kg diet	<i>Recommended test concentrations include at least two concentrations other than the control; three or more will provide a better statistical analysis. The highest test concentrations should show a significant effect or be at or above the actual or expected field residue level.</i>
Maximum labeled field residue anticipated and source of information:	Not specified	<i>The highest test concentrations should show a significant effect or be at or above the actual or expected field residue level. The source (i.e., maximum label rate in lb ai/A and ppm), label registration no., label date, and site should be cited]</i>
<u>Solvent/vehicle, if used</u> Type: Amount:	None N/A	<i>Recommended solvents include corn oil or other appropriate vehicle not more than 2% of diet by weight</i>
Was detailed description and nutrient analysis of the basal diet provided? (Yes/No)	Yes	<i>A commercial breeder feed or an equivalent that is appropriate for the test species is recommended.</i>
Preparation of test diet	For each level, test substance was mixed into a premix basal feed. Test diets were prepared weekly beginning August 2, 2011 and presented to birds on Tuesday of each week.	<i>A premixed diet containing the test substance should be mechanically mixed with basal diet. If an evaporative vehicle is used, it should be completely evaporated prior to feeding.</i>
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes	See Reviewer's Comments section.
Were concentrations in diet verified by chemical analysis?	Yes	See Reviewer's Comments section.

Parameter	Details	Remarks
		Criteria
Did chemical analysis confirm that diet was stable?	Yes	See Reviewer's Comments section.
Homogeneous?	Yes	
Feeding and husbandry	Feeding and husbandry conditions appeared to be adequate, given guideline recommendations.	
<u>Test conditions (pre-laying)</u> Temperature: Relative humidity: Photoperiod:	22.6 ± 1.1°C 64 ± 16% 8 hr light/day through Week 8; 17 hr light/day thereafter	Light intensity was 268 lux. <i>Recommended temperature: about 21°C (70°F)</i> <i>Recommended relative humidity: about 55%</i> <i>Recommended lighting</i> <i>First 8 weeks: 7 h per day.</i> <i>Thereafter: 16-17 h per day.</i> <i>At least 6 foot-candles are recommended at bird level.</i>
Egg Collection and Incubation		
<u>Egg collection and storage</u> Collection interval: Storage temperature: Storage humidity:	Daily 14.2 ± 0.1°C 85 ± 5%	<i>Eggs should be collected daily; recommended egg storage temperature is approximately 16°C (61°F); recommended humidity is approximately 65%.</i> <i>Recommended collection interval: daily</i>
Were eggs candled for cracks prior to setting for incubation?	Yes	<i>Eggs should be candled on day 0</i>
Were eggs set weekly?	Yes	
When candling was done for fertility?	Eggs were candled again on Days 14 (embryo viability) and 20-21 (embryo survival).	<i>Quail: approx. day 11</i> <i>Ducks: approx. day 14</i>
When the eggs were transferred to the hatcher?	Day 24	<i>Bobwhite: usually day 21</i> <i>Mallard: usually day 23</i>

Parameter	Details	Remarks
		Criteria
<u>Hatching conditions</u> Temperature: Humidity: Photoperiod:	37.3 ± 0.0°C 60 ± 0% 17 hours light/day	<i>Recommended temperature is 39°C (102°F) Recommended humidity is 70%</i>
Day the hatched eggs were removed and counted	Day 27-28	<i>Eggs for bobwhite should be removed on day 24; for Mallard on day 27</i>
Were egg shells washed and dried for at least 48 hrs before measuring?	Yes	
<u>Egg shell thickness</u> No. of eggs used: Intervals: Mode of measurement:	One egg from each of the odd numbered pens during odd numbered weeks and one egg from each of the even numbered pens during even numbered weeks were collected and measured. Weekly Five points around the waist of the egg using a micrometer to the nearest 0.002 mm.	<i>Newly hatched eggs should be collected at least once every two weeks. Thickness of the shell plus membrane should be measured to the nearest 0.01 mm with 3 - 4 measurements per shell.</i>
Reference chemical, if used	None used.	

2. Observations:

Table 3: Observations

Parameter	Details	Remarks
Parameters measured		
<u>Parental</u> (mortality, body weight, mean feed consumption) <u>Egg collection and subsequent development</u> (no. of eggs laid, no. of eggs cracked, shell thickness, no. of eggs set, no. of viable embryos, no. of live 3 week embryos, no. hatched, no. of 14-day survivors, average weight of 14-d old survivors, mortality, gross pathology, others)	- mortality - signs of toxicity - body weight - feed consumption - eggs laid - eggs cracked - egg shell thickness - eggs set - viable embryos - live 3-week embryos - hatchlings - hatchling body weight - 14-day-old survivors - 14-day-old survivor body weight	<i>Recommended endpoints measured include:</i> <ul style="list-style-type: none"> • Eggs laid/pen • Eggs cracked/pen • Eggs set/pen • Viable embryos/pen • Live 3-week embryos/pen • Normal hatchlings/pen • 14-day-old survivors/pen • 14-day-old survivors/pen • Weights of 14-day-old survivors (mean per pen) • Egg shell thickness • Food consumption (mean per pen) • Initial and final body weight (mean per pen)
Indicate if the test material was regurgitated	No indications of dietary regurgitation.	
Observation intervals (for various parameters)	Parental mortality and signs of toxicity were recorded daily. Parental body weights were recorded on Weeks 0, 2, 4, 6, 8, and at adult termination. Offspring were weighed when removed from the hatcher and at 14 days. Parental feed consumption was measured weekly.	<i>Body weights and food consumption should be measured at least biweekly</i>
Were raw data included?	Yes	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortalities occurred in the control or treatment groups.

B. REPRODUCTIVE AND OTHER ENDPOINTS:

Abnormal Effects/Behavior: No treatment-related signs of toxicity were observed during the study. The incidental clinical observations of feather loss, molting, foot lesions, lameness, crusty eyes, swollen abdomen, and unkempt were associated with injuries and pen wear. All other birds were normal in appearance and behavior.

No treatment-related findings were observed in the ≤ 18.2 mg ai/kg diet groups based on the gross necropsy results. At 100 mg ai/kg, the treatment-related finding of enlarged thyroids was observed during necropsy.

Food Consumption: No significant treatment-related differences in food consumption were observed during the study. The estimated overall mean dietary doses were 0.0, 0.5, 2.6, and 13.6 mg ai/kg/day for the control, 4, 20, and 100 mg ai/kg groups, respectively.

Body Weight: No significant treatment-related differences were observed between the control group and any of the treatment groups at any of the adult body weight intervals. No treatment-related effects on offspring body weight were observed in any treatment groups.

Reproductive Effects: No significant treatment-related differences in any reproductive parameter were observed during the study.

No significant treatment-related differences in egg shell thickness were observed between the control group and any of the treatment groups.

Table 4: Reproductive and Other Parameters (nominal concentrations; study author-reported).

Parameter	Control	4 mg ai/kg	20 mg ai/kg	100 mg ai/kg	NOAEC/ LOAEC
No. laying pairs	16	16	16	16	100 mg ai/kg >100 mg ai/kg
Eggs laid/pair	806	775	818	837	100 mg ai/kg >100 mg ai/kg
Eggs cracked/pair	1	0	3	2	100 mg ai/kg >100 mg ai/kg
Eggs set/pair	722	695	739	758	100 mg ai/kg >100 mg ai/kg
Viable embryos/pair	666	652	670	652	100 mg ai/kg >100 mg ai/kg
Live 3-week embryos/pair	666	647	668	643	100 mg ai/kg >100 mg ai/kg
Hatchlings/pair	580	549	620	544	100 mg ai/kg >100 mg ai/kg
14-day old hatchling	577	548	612	540	100 mg ai/kg

Parameter	Control	4 mg ai/kg	20 mg ai/kg	100 mg ai/kg	NOAEC/ LOAEC
survivors/pair					>100 mg ai/kg
Eggs laid/hen	50	48	51	52	100 mg ai/kg >100 mg ai/kg
Eggs laid/hen/day (83 days)	0.61	0.58	0.62	0.63	100 mg ai/kg >100 mg ai/kg
14-day old survivors/hen	36	34	38	34	100 mg ai/kg >100 mg ai/kg
Eggs laid/maximum laid (%)	73	70	74	76	100 mg ai/kg >100 mg ai/kg
Eggs cracked/eggs laid (%)	0	0	0	0	100 mg ai/kg >100 mg ai/kg
Viable embryos/eggs set (%)	92	94	91	87	100 mg ai/kg >100 mg ai/kg
Live 3-week embryos/viable embryos (%)	100	99	100	98	100 mg ai/kg >100 mg ai/kg
Hatchlings/Live 3-week embryos (%)	88	84	92	84	100 mg ai/kg >100 mg ai/kg
14-day old survivors/Hatchlings (%)	99	100	98	99	100 mg ai/kg >100 mg ai/kg
Hatchlings/Eggs set (%)	81	78	84	73	100 mg ai/kg >100 mg ai/kg
14-Day old survivors/Eggs set (%)	80	78	83	72	100 mg ai/kg >100 mg ai/kg
Hatchlings/Maximum set (%)	59	56	63	56	100 mg ai/kg >100 mg ai/kg
14-Day old survivors/Maximum set (%)	59	56	63	55	100 mg ai/kg >100 mg ai/kg
Shell thickness (mm \pm SD)	0.398 \pm 0.017	0.398 \pm 0.018	0.387 \pm 0.019	0.395 \pm 0.017	100 mg ai/kg >100 mg ai/kg
Hatchling weight (g \pm SD)	34 \pm 2	34 \pm 3	36 \pm 2	35 \pm 3	100 mg ai/kg >100 mg ai/kg
14-day old survivors weight (g \pm SD)	312 \pm 16	316 \pm 20	318 \pm 18	321 \pm 16	100 mg ai/kg >100 mg ai/kg

Parameter	Control	4 mg ai/kg	20 mg ai/kg	100 mg ai/kg	NOAEC/ LOAEC
Mean food consumption (g/bird/day)	139	147	144	147	100 mg ai/kg >100 mg ai/kg
Weight (g) of parent females at test initiation: at Week 4: at test termination:	1025 1051 1192	1053 1041 1185	1022 1042 1172	1020 1029 1140	100 mg ai/kg >100 mg ai/kg
Weight (g) of parent males at test initiation: at Week 4: at test termination:	1128 1148 1168	1141 1157 1156	1135 1135 1160	1133 1144 1134	100 mg ai/kg >100 mg ai/kg

^a Data obtained from Page 22, Table 1 on page 25, Table 3 on page 30, Table 4 on page 32, Table 5 on page 34, and Table 6 on page 35 of the study report.

C. REPORTED STATISTICS:

Each of the treatment groups was compared to the control group using an analysis of variance (ANOVA) followed by Dunnett's Multiple Comparison Procedure. Sample units were the individual pens within each experimental group, except adult body weights, where the sample unit was the individual bird. Percentage data were arcsine square root transformed prior to analysis. Nominal concentrations were used for all analyses.

D. VERIFICATION OF STATISTICAL RESULTS:

Statistical Method: Data were tested to determine if they satisfied the assumptions of normality using Shapiro-Wilks test and homogeneity of variances using Bartlett's test. Eggshell thickness, hatchling weight, 14-d survivor weight, food consumption, and female weight gain met these assumptions of parametric statistics and was therefore analyzed using Dunnett's multiple comparison test. A suggestive decreasing monotonic response was noted for male weight gain and live embryos per egg set; the responses were not linear, though overall decreasing trends were exhibited. The Jonckheere-Terpstra Step-Down Test was used to analyze live embryos per egg set and Williams test was used to analyze male weight gain. The Wilcoxon test with Bonferroni Adj was used to determine the NOAEL/LOAEL values for all endpoints which were non-parametric data that did not exhibit a monotonic response. Unless otherwise indicated, effects were considered statistically significant at $p < 0.05$. These analyses were conducted using CETIS version 1.8.7.12 with backend settings approved for use by EFED on 5/29/13. Analyses were conducted using mean-measured concentrations.

NOAEC: 100 mg ai/kg
LOAEC: >100 mg ai/kg
Endpoint(s) affected: None

Table 5: Reproductive and Other Parameters (mean-measured concentrations; reviewer-reported).

Parameter	Control	3.50 mg ai/kg	18.2 mg ai/kg	100 mg ai/kg	NOAEC/ LOAEC
Eggs laid/pen	50.4	48.4	51.1	52.3	100 mg ai/kg >100 mg ai/kg
Eggs not cracked/eggs laid (%)	99.9	100	99.7	99.8	100 mg ai/kg >100 mg ai/kg
Shell thickness (mm)	0.398	0.398	0.387	0.395	100 mg ai/kg >100 mg ai/kg
Viable embryos/eggs set (%)	92.4	94.0	91.0	86.7	100 mg ai/kg >100 mg ai/kg
Live embryos/eggs set (%)	92.4	92.9	90.7	85.5	100 mg ai/kg >100 mg ai/kg
No. of hatchlings/eggs set (%)	80.7	78.2	84.0	72.8	100 mg ai/kg >100 mg ai/kg
14 Day hatchlings/eggs set (%)	80.3	78.0	83.0	72.3	100 mg ai/kg >100 mg ai/kg
Live embryos/viable embryos (%)	100	98.9	99.7	98.2	100 mg ai/kg >100 mg ai/kg
Hatchling/live embryos (%)	87.7	83.9	92.3	83.9	100 mg ai/kg >100 mg ai/kg
14 Day hatchling/no. hatched (%)	99.4	99.9	98.0	99.3	100 mg ai/kg >100 mg ai/kg
Hatchling weight (g)	33.6	34.4	35.6	35.0	100 mg ai/kg >100 mg ai/kg
14 Day survivor weight (g)	312	316	318	321	100 mg ai/kg >100 mg ai/kg
Mean food consumption (g/bird/day)	139	147	144	147	100 mg ai/kg >100 mg ai/kg
Male weight gain (g)	40.1	13.9	25.8	1.5	100 mg ai/kg >100 mg ai/kg
Female weight gain (g)	167	132	150	120	100 mg ai/kg >100 mg ai/kg

* Statistically different from the control at $p < 0.05$.

** Statistically different from the control at $p < 0.01$.

E. STUDY DEFICIENCIES:

This study is scientifically sound and there were no study deficiencies.
No deviations from OCSPP guideline 850.2300 were noted.

F. REVIEWER'S COMMENTS:

The reviewer's results were comparable to those of the study authors. Though not statistically analyzed, the reviewer agrees that enlarged thyroids in all but one bird at the highest treatment level are likely treatment-related. Mean-measured concentrations are reported in the Executive Summary and Conclusions sections of the DER.

Despite the large reductions in male body weight gain, the reviewer and study authors failed to detect significant differences relative to the negative control. The control and treatment groups exhibited comparable ranges and standard errors and the high degree of variability likely precluded the detection of significant differences.

All validity requirements were met. Specifically, controls produced an average of thirty-six (36) 14-day old survivors per hen during the 10-week production phase (minimum of 12 chicks per pen during a 10-week production phase), the egg shell thickness of control eggs was 0.398 mm (minimum of 0.34 mm for Mallards), and adult control mortality was <10%.

Homogeneity, stability, and concentration verification samples were analyzed for Ethylenethiourea concentrations during the definitive study and were included in the study report. The coefficients of variation were 4.22-6.65% for the homogeneity samples. The stability samples at Day 7 were 96-99% of the Day 0 values. The test concentrations were 88-100% of nominal for the verification samples.

Experimental test dates were August 2, 2011-February 2, 2012.

G. CONCLUSIONS:

This study is scientifically sound and acceptable for use in Agency risk assessments. No mortalities or treatment-related signs of toxicity were observed in the control or treatment groups. No treatment-related findings were observed in the ≤ 18.2 mg ai/kg diet groups based on the gross necropsy results. At 100 mg ai/kg, the treatment-related finding of enlarged thyroids was observed during necropsy. There were no treatment-related differences in feed consumption, adult body weights, or offspring body weights at any treatment level. No apparent treatment-related effects on reproduction were observed during the study. No significant treatment-related differences in egg shell thickness were observed between the control group and any of the treatment groups. The NOAEC was 18.2 mg ai/kg diet (mean-measured concentration) based on the necropsy finding of enlarged thyroids.

Reproductive and Growth Endpoints:

NOAEC: 100 mg ai/kg (mean-measured)

LOAEC: >100 mg ai/kg (mean-measured)

Non Reproductive Effects noted: Enlarged Thyroid glands in highest dose group

NOAEC: 18.2 mg ai/kg (mean-measured)

LOAEC: 100 mg ai/kg (mean-measured)

III. REFERENCES: None; other than standard guidelines and methodologies.